

REMARKS

Applicants have amended claims 1, 8-10, and 18, have added new claim 21 and have canceled claim 2 and 15-17 without prejudice to or disclaimer of the subject matter contained therein. As such, claims 1, 3-14 and 18-21 are currently pending in the present application.

New claim 21 has basis in the present specification at page 4 in the last 2 paragraphs.

No new matter has been introduced to the claims within the meaning of 35 U.S.C. §132. Accordingly, entry of the amendments is respectfully requested and further and favorable consideration is earnestly solicited in view of the following remarks.

1. Rejection of Claims 3-14 under 35 U.S.C. §112, 2nd Paragraph

The Official Action states that claims 3-14 are rejected under 35 U.S.C. §112, 2nd paragraph as being indefinite.

In particular, the Official Action states that “claims 3-14 recite the limitation ‘for application to the mucosa according to claim 1 and/or claim 11’ in claims 3-14 and the limitation ‘said water-insoluble and/or water-low soluble substances’ in claim 8. There is insufficient antecedent basis for these limitations in the claim.”

Applicants have amended claim 1 to also recite “for application to the mucosa”. Accordingly, sufficient antecedent basis exists for this claim limitation in the rejected claims.

Applicants have also amended claims 8-10 and have added new claim 21 to

ensure proper antecedent basis exists for the claimed subject matter.

Applicants submit that the aforementioned amendments render this rejection moot. As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of pending claims 3-14.

2. Rejection of Claims 1, 3-16, 18 and 20 under 35 U.S.C. §103(a)

The Official Action states that claims 1, 3-16, 18 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Magee et al. (US Application Publication 2002/0111495).

As the basis of the rejection, the Official Action states in relevant part:

Magee et al. teaches the use of selective PDE4 inhibitors for improved therapeutic treatment of a number of inflammatory, respiratory and allergic diseases including chronic rhinitis. Magee et al. further teaches that the present compounds can be used together in combination with one or more therapeutic agents including antihistaminic H2 receptor antagonists such as azelastine, the steroid ciclesonide and with pharmaceutically [sic] carriers. The compositions of Magee et al. can be administered to humans. Magee et al. also teaches the route of administration that can critically affect bioavailability, solubility of the active agents and rapid absorption. By carriers, Magee et al. teaches addition of acceptable diluents, adjuvants, vehicles [sic] viscosity modifiers and other agents known to the artisan for providing favorable properties to the final pharmaceutical composition including water as a solvent, salts such as sodium chloride for isotonic properties (i.e. osmotic pressure-controlling agent; instant claim 7), cellulose-based substances such as sodium carboxymethylcellulose, polyethylene glycol as a wetting agent, polyethylene polyoxypropylene block polymer as a surfactant, emollients, humectants such as glycerin (instant claim 13), surfactants and sugars such as glucose. Magee et al. further teaches the composition for intranasal application.

Magee et al. does not particularly teach a composition with a particular osmotic pressure or a composition containing microcrystalline cellulose as solid particles in an aqueous medium.

However, Magee et al. does teach the inclusion of water-low soluble substance such as cellulose derivatives which encompasses all substances containing cellulose including microcrystalline cellulose [(MCC)] which are solid particles before addition to the pharmaceutical composition. Moreover, Magee et al. teaches the use of viscosity modifiers and given that [MCC] is a well-known viscosity modifier, one of ordinary skill would readily add such compound as solid particles as to obtain the desired product with the desired osmotic pressure. Additionally, Magee et al. teaches the addition of osmotic pressure controlling agents including glucose and sodium chloride. Consequently, these agents would necessarily affect the osmotic pressure of the composition due to their isotonicization properties. Thus, to acquire the desired osmotic pressure for enhancing the bioavailability of the active ingredients as suggested by Magee et al., one of ordinary skill would be motivated to vary the concentration of the osmotic pressure controlling agents in a particular form of the composition.

RESPONSE

First, Applicants respectfully note that claims 15-16 have been canceled without prejudice to or disclaimer of the subject matter contained therein, rendering the basis for the rejection of these claims moot.

With regards to presently pending claims 1, 3-14, 18 and 20, Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary

skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." See *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Applicants respectfully submit that the broadest independent claim, claim 1, has been amended to recite "[a] pharmaceutical composition for application to the mucosa comprising as active ingredients a combination of 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl)-1(2H)phthalazinone (AZELASTINE) ~~at least one~~ antihistamine, or a stereoisomer, a pharmaceutically acceptable salt or physiologically functional derivative thereof, and ciclesonide, or a pharmaceutically acceptable salt of ciclesonide, an epimer of ciclesonide, or a physiologically functional derivative of ciclesonide, and a pharmaceutically acceptable carrier and/or one or more excipients,

wherein said pharmaceutical composition has an osmotic pressure of less than 290 mOsm.”

The Examiner has relied on the Magee et al. reference in the rejection of presently pending claims 1, 3-14, 18 and 20.

For the sake of brevity, applicants have minimized their discussion of previously filed arguments regarding the substance of this rejection. However, applicants incorporate those arguments by reference in their entirety.

Further, applicants respectfully point out to the Examiner that Magee et al. teach the optional combination of a broad genus of PDE4 inhibitors with many various additional active ingredients selected from quite a large “laundry list”. See Magee et al., [0218]. Applicants again respectfully point out to the Examiner that no PDE4 inhibitor is presently claimed.

Applicants further respectfully point out to the Examiner that claim 1 has been amended to recite two specific active ingredients – azelastine or a stereoisomer, a pharmaceutically acceptable salt or physiologically functional derivative thereof; and ciclesonide, or a pharmaceutically acceptable salt of ciclesonide, an epimer of ciclesonide, or a physiologically functional derivative of ciclesonide.

In view of this amendment, applicants respectfully submit that the presently pending claims are not obvious over the Magee et al. reference. Indeed, the Magee et al. reference has absolutely no teaching that would motivate the skilled artisan to pick and choose the two presently claimed active ingredients from the “additional active ingredient” list contained in Magee et al. at [0218]. Further, none of the Examples of Magee et al. contain even a PDE4 inhibitor combined with the presently claimed

combination. Therefore, a person of ordinary skill in the art would have to modify the Magee et al. reference to arrive at the presently claimed combination. This modification is not taught in the Magee et al. reference. Accordingly, a person of ordinary skill in the art would not have any expectation of success in arriving at the presently pending claims. Therefore, no *prima facie* case of obviousness can exist against the presently pending claims since the requirements of *Amgen Inc. v. Chugai Pharm. Co.*, supra, have not been met.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claims because the Magee et al. reference clearly fails to provide any motivation to the skilled artisan to pick and choose the two compounds presently claimed. Further, even if the skilled artisan were so motivated to pick just the two recited compounds in the presently claimed composition, there would be no expectation of success of such a combination.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claims 1, 3-14, 18 and 20.

3. Rejection of Claim 19 under 35 U.S.C. §103(a)

The Official Action states that claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over Magee et al. (US Application Publication 2002/0111495) in view of Calatayud et al. (US Patent No. 5,482,934)

RESPONSE

Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claim.

For the sake of brevity, Applicants' arguments regarding the Magee et al. reference outlined in section 2 above are incorporated by reference in their entirety.

The Calatayud et al. reference does not remedy the deficient teachings of the Magee et al. reference. Calatayud et al. do not provide any motivation to the skilled artisan to pick and choose the two compounds presently claimed. Further, even if the skilled artisan were so motivated to pick just the two recited compounds in the presently claimed composition, there would be no expectation of success of such a combination.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claim 19.

4. Rejection of Claims 1-16, 18 and 20 under 35 U.S.C. §103(a)

The Official Action states that claims 1-16, 18 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Szelenyi et al. (WO01/22955-corresponding to US Patent No. 7,022,687) in view of Schmidt et al.

RESPONSE

Again, Applicants respectfully note that claims 15-16 have been canceled without prejudice to or disclaimer of the subject matter contained therein, rendering the basis for the rejection of these claims moot.

With regards to presently pending claims 1, 3-14, 18 and 20, Applicants

respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims.

Similar to the Magee et al. reference discussed above in section 2, the Szelenyl et al. reference does not provide any motivation to the skilled artisan to pick and choose the two compounds presently claimed. Further, even if the skilled artisan were so motivated to pick just the two recited compounds in the presently claimed composition, there would be no expectation of success of such a combination based on the disclosure of Szelenyl.

The Schmidt et al. reference does not remedy the deficient teachings of the Szelenyl et al. reference. Schmidt et al. do not provide any motivation to pick and choose the two compounds presently claimed. Further, even if the skilled artisan were so motivated to pick just the two recited compounds in the presently claimed composition, there would be no expectation of success of such a combination based on the disclosures of Szelenyl and/or Schmidt et al.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claims 1, 3-14, 18 and 20.

5. Rejection of Claim 19 under 35 U.S.C. §103(a)

The Official Action states that claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over Szelenyl et al. in view of Schmidt et al. and further in view of Calatayud et al.

RESPONSE

Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claim.

For the sake of brevity, Applicants' arguments regarding the Szelenyl et al. and Schmidt et al. references outlined in section 4 above are incorporated by reference in their entirety.

The Calatayud et al. reference does not remedy the deficient teachings of these references. As stated above in section 3, Calatayud et al. do not provide any teaching that would motivate the skilled artisan to pick and choose the two compounds presently claimed. Further, even if the skilled artisan were so motivated to pick just the two recited compounds in the presently claimed composition, there would be no expectation of success of such a combination.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claim 19.

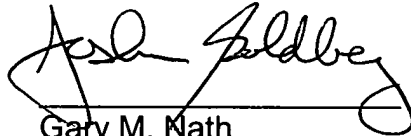
CONCLUSION

Based upon the remarks, the presently claimed subject matter is believed to be patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the outstanding rejections and allow all pending claims 1, 3-14 and 18-21. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if he has any questions or comments. The Examiner is specifically authorized to charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP

A handwritten signature in black ink, appearing to read "Gary M. Nath", written over a horizontal line.

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